Smallpox Bibliography
October 2003

1: Acad Emerg Med. 2003 Jun;10(6):599-605.

Emergency physicians' perspectives on smallpox vaccination.

Kwon N, Raven MC, Chiang WK, Moran GJ, Jui J, Carter RA, Goldfrank L; EMERGEncy ID Net Study Group.

Bellevue Hospital/NYU Medical Center, New York, NY, USA.

OBJECTIVE: To evaluate emergency physician (EP) attitudes toward smallpox vaccination, the treatment of patients with suspected smallpox, and the threat of a bioterrorist attack. METHODS: This was a prospective study utilizing a standardized survey instrument that was distributed on November 16, 2002, and collected by February 1, 2003. EPs from a sample of 50 accredited emergency medicine programs were surveyed regarding their perspectives on smallpox vaccination. RESULTS: A total of 989 surveys were collected from 42 emergency medicine programs. Of the respondents, 43.4% would currently volunteer for smallpox vaccination. EPs previously vaccinated against smallpox were 1.46 times more likely to volunteer for vaccination (95% CI = 1.14 to 1.93). EPs who believed they were at risk for complications were less than half as likely to volunteer for vaccination. EPs who perceived a significant risk of a bioterrorist attack were 2.7 times more likely to volunteer for the vaccine compared with those who thought the risk was minimal (95% CI = 2.06 to 3.47). Of the respondents, 34.4% believed the risks of the vaccination outweighed the benefits, 33% did not, and 32.6% were unsure. CONCLUSIONS: Currently, fewer than
half of EPs surveyed would volunteer for smallpox vaccination. Factors associated with a willingness to be vaccinated include previous smallpox vaccination and the perceived threat of a bioterrorist attack. The variation in EP attitudes toward smallpox vaccination may be due to uncertain risk-to-benefit ratio. The opinions and actions of EPs may be influential on current and future government policy and public opinion.

PMID: 12782519 [PubMed - indexed for MEDLINE]

2: Acad Emerg Med. 2003 Jun;10(6):606-11.

Smallpox vaccination: a national survey of emergency health care providers.

Everett WW, Coffin SE, Zaoutis T, Halpern SD, Strom BL.

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Concerns about bioterrorism have prompted a national voluntary smallpox (SP) vaccination program in the United States. Although emergency health care providers are among the first targeted for vaccination, little is known about how these providers view the risks and benefits of SP vaccination. OBJECTIVES: To assess the willingness of emergency health care personnel to receive pre-event SP vaccination prior to the start of the national program. METHODS: The authors conducted a national cross-sectional, anonymous survey of 1,701 emergency physicians, nurses, and mid-level practitioners working full time in 13 adult and pediatric academic emergency departments in large U.S. cities in November and December 2002. The main outcome measure was willingness to be vaccinated against SP. Secondary outcomes included the prevalence of self-reported contraindications, and reasons for and against vaccination. RESULTS: 732 emergency health care providers returned questionnaires (response rate 43%). Overall, 73% (95% CI = 66% to 80%) were willing to receive pre-event SP vaccination. 18% (95% CI = 14% to 23%) reported contraindications to vaccination, and 50% (95% CI = 39% to 61%) of these providers were willing to receive pre-event SP vaccination. Self-protection (72%) was the most common reason cited for desiring vaccination against SP; concern about vaccine-related adverse events (54%) was the most common reason cited for not wanting immunization. CONCLUSIONS: Most emergency health care providers express a willingness to receive pre-event SP immunization; self-protection is a principal motivating reason. A subset of health care providers, however, may place themselves at increased risk by desiring vaccination despite contraindications.

PMID: 12782520 [PubMed - indexed for MEDLINE]

3: Acad Emerg Med. 2003 Jun;10(6):681-3.

Smallpox vaccination for emergency physicians.

AAEM/SAEM Smallpox Vaccination Working Group.

On December 13, 2002, President Bush formally announced the national smallpox vaccination program. The plan involves vaccinating health care workers who would respond to possible smallpox cases, including emergency physicians. Although not all aspects of the program are clearly established, it appears that vaccination of health care workers will occur in the near future. This joint statement has been used by the American Academy of Emergency Medicine and the Society for Academic Emergency Medicine regarding smallpox vaccination for emergency physicians.

Publication Types:
Guideline

PMID: 12782532 [PubMed - indexed for MEDLINE]

4: Am J Health Syst Pharm. 2003 Apr 15;60(8):749-56; quiz 757-8.

Smallpox: a review of clinical disease and vaccination.

Lofquist JM, Weimert NA, Hayney MS.

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The clinical course of smallpox infection and the current and future roles of vaccination and strategies for controlling smallpox outbreaks are reviewed. Close personal contact is required for transmission of variola, the DNA virus that causes smallpox. Following an incubation period, infected persons have prodromal symptoms that include high fever, back pain, malaise, and prostration. The eruptive stage is characterized by maculopapular rash that progresses to papules, then vesicles, and then pustules and scab lesions. The mortality rate for smallpox is approximately 30%. Patients having a fever and rash may be confused with having chickenpox. The most effective method for preventing smallpox epidemic progression is vaccination. Until recently, only 15 million doses of smallpox vaccine--manufactured 20 years ago--were available in the United States. The vaccine is a live vaccinia virus preparation administered by scarification with a bifurcated needle. The immune response is protective against orthopoxviruses, including variola. Vaccination is associated with moderate to severe complications, such as generalized vaccinia, eczema vaccinatum, progressive vaccinia, and postvaccinial encephalitis. Efforts for vaccine production are now focused on a live cell-culture-derived vaccinia virus vaccine. Although smallpox was eradicated in 1980, it remains a potential agent for bioterrorism. As a category A biological weapon, its potential to devastate populations causes concern among those in the public health community who have been actively developing plants to deal with smallpox and other potential agents of biological warfare. The only proven effective strategy against smallpox is vaccination.

Publication Types:
Review
Review, Tutorial

PMID: 12749161 [PubMed - indexed for MEDLINE]

5: Antiviral Res. 2003 Apr;58(2):101-14.

Pathogenesis and potential antiviral therapy of complications of smallpox vaccination.

Bray M.

Biodefense Clinical Research Branch, Office of Clinical Research, National Institute of Allergy and Infectious Disease, National Institutes of Health, Bethesda, MD 20892, USA. mbray@niaid.nih.gov

Vaccination against smallpox may result in a variety of complications, ranging in severity from benign to lethal. Universal vaccination was halted in the US in

1972, so almost half the present population has never been vaccinated. Because side effects occur most often in first-time vaccinees, current plans for rapid large-scale vaccination in the event of bioterrorist attack raise concerns about the occurrence of a large number of adverse events. Most complications result from the excessive replication of vaccinia virus, making them potential targets for antiviral therapy. Effective treatment is especially needed for persons with atopic dermatitis or eczema, who are unusually susceptible to the initiation and spread of vaccinia infection because of defects of innate immunity in the skin, and for individuals with defective cell-mediated immunity, who are unable to eliminate vaccinia infection once it has begun. In the past, many complications were treated with vaccinia immune globulin (VIG) and/or the antiviral drug methisazone, but neither was tested in placebo-controlled trials. New antiviral drugs are now available, but have not yet been evaluated for treating vaccinia infections in humans. Both laboratory research and clinical studies are needed to help prevent serious complications in any major vaccination campaign.

Publication Types:
Review
Review, Tutorial

PMID: 12742570 [PubMed - indexed for MEDLINE]

6: BMJ. 2003 Sep 27;327(7417):699.

Claim that smallpox vaccine protects against HIV is premature, say critics.

Lenzer J.

Publication Types:
News

PMID: 14512458 [PubMed - indexed for MEDLINE]

7: Clin Med. 2003 May-Jun;3(3):255-9.

Anticipating smallpox as a bioterrorist weapon.

Mortimer PP.

Virus Reference Division, Central Public Health Laboratory, London.
PMortimer@PHLS.org.uk

The treat of bioterrorism means it is important to be able to diagnose smallpox. The responsibility for the initial recognition of cases lies with clinicians, and early diagnosis is the key to the successful control of an outbreak. Unless rapidly contained, a bioterrorist release of smallpox would constitute not just a national but a global threat to health. This brief review sets smallpox in its modern context as an infection potentially spread by bioterrorists and recommends sources of information from the twentieth century that will assist clinicians in diagnosing the disease.

Publication Types:
Review
Review, Tutorial

PMID: 12848261 [PubMed - indexed for MEDLINE]

8: Crit Rev Microbiol. 2003;29(2):79-190.

The 1971 smallpox outbreak in the Soviet city of Aralsk: Implications for Variola virus as a bioterrorist threat. Proceedings of special issue.

[No authors listed]

Publication Types:
Historical Article
Overall

PMID: 14531392 [PubMed - indexed for MEDLINE]

9: Crit Rev Microbiol. 2003;29(2):177-82; discussion 183-90.

Commentary on Dr. Alan P. Zelicoff's analysis (No. 7).

Woodall J.

Nucleus for the Investigation of Emerging Infectious Diseases, Department of Medical Biochemistry, Institute of BiomedicalSciences, Federal University of Rio de Janeiro, Brazil.

Publication Types:
Historical Article

PMID: 12901686 [PubMed - indexed for MEDLINE]

10: Crit Rev Microbiol. 2003;29(2):175-6; discussion 183-90.

Commentary on Dr. Alan P. Zelicoff's analysis (No. 6).

Popov S.

Hadron Corporation, USA.

Publication Types:
Historical Article

PMID: 12901685 [PubMed - indexed for MEDLINE]

11: Crit Rev Microbiol. 2003;29(2):173-4; discussion 183-90.

Commentary on Dr. Alan P. Zelicoff's analysis (No. 5).

Merkle PB.

Sandia National Laboratories, Albuquerque, New Mexico, USA.

Publication Types:
Historical Article
Review
Review, Tutorial

PMID: 12901684 [PubMed - indexed for MEDLINE]

12: Crit Rev Microbiol. 2003;29(2):171-2; discussion 183-90.

Commentary on Dr. Alan zelicoff's Analysis of the Aralsk outbreak (No. 4).

Jahrling PB.

U.S. Army Medical Research Institute of Infectious Disease, 1425 Porter Street, Frederick, MD 21702-5011, USA.

Publication Types:
Historical Article

PMID: 12901683 [PubMed - indexed for MEDLINE]

13: Crit Rev Microbiol. 2003;29(2):81-95.

The 1971 smallpox outbreak in the Soviet city of Aralsk: implications for Variola virus as a bioterrorist threat. Introduction.

Tucker JB, Zilinskas RA.

Chemical and Biological Weapons Nonproliferation Program, Center for Nonproliferation Studies, Monterey Institute of International Studies. USA.

Publication Types:
Historical Article

PMID: 12901676 [PubMed - indexed for MEDLINE]

14: Crit Rev Microbiol. 2003;29(2):145-8; discussion 153-8.

Report on measures taken to contain and eradicate the smallpox outbreak locale in the city of Aralsk, Part II.

Sarynov E, Kulmakhanov B.

Publication Types:
Historical Article

PMID: 12901679 [PubMed - indexed for MEDLINE]

15: Crit Rev Microbiol. 2003;29(2):159-61; discussion 183-90.

Commentary on implications of the 1971 outbreak in Aralsk, Kazakhstan, for U.S. Smallpox Vaccination Policy (No. 1).

Atlas RM, Clover R.

University of Louisville, University of Louisville, Louisville KY 40292, USA.

Publication Types:
Historical Article

PMID: 12901680 [PubMed - indexed for MEDLINE]

16: Crit Rev Microbiol. 2003;29(2):163-7; discussion 183-90.

Commentary on the 1971 smallpox epidemic in Aralsk, Kazakhstan, and the Soviet Biological Warfare Program (No. 2).

Gilsdorf JR.

Pediatric Infectious Diseases, University of Michigan Medical Center, L2225 Women's Hospital, Ann Arbor, Michigan 48109-0244, USA.

Publication Types:
Historical Article

PMID: 12901681 [PubMed - indexed for MEDLINE]

17: Crit Rev Microbiol. 2003;29(2):109-44; discussion 149-52.

Report on measures taken to contain and eradicate the smallpox outbreak locale in the city of Aralsk (September/October, 1971).

Sarynov E, Kulmakhanov B, Makatov Z.

Publication Types:
Historical Article

PMID: 12901678 [PubMed - indexed for MEDLINE]

18: Crit Rev Microbiol. 2003;29(2):169-70; discussion 183-90.

Commentary on Dr. Alan Zelicoff's epidemiological analysis of the Aralsk outbreak (No. 3).

Henderson DA.

Center for Civilian Biodefense Strategies, The Johns Hopkins University, Baltimore, Maryland, USA.

Publication Types:
Historical Article

PMID: 12901682 [PubMed - indexed for MEDLINE]

19: Crit Rev Microbiol. 2003;29(2):97-108.

An epidemiological analysis of the 1971 smallpox outbreak in Aralsk, Kazakhstan.

Zelicoff AP.

Sandia National Laboratories.

Publication Types:
Historical Article

PMID: 12901677 [PubMed - indexed for MEDLINE]

20: Expert Rev Vaccines. 2002 Jun;1(1):5.

NIH study supports diluting smallpox vaccine stockpile.

[No authors listed]

Publication Types:
News

PMID: 12908505 [PubMed - indexed for MEDLINE]

21: Fed Regist. 2003 Aug 27;68(166):51492-9.

Smallpox Vaccine Injury Compensation Program: Smallpox (Vaccinia) Vaccine Injury Table. Interim final rule.

Health Resources and Services Administration, HHS.

The Smallpox Emergency Personnel Protection Act of 2003 (SEPPA), Public Law 108-20, 117 Stat. 638, authorized the Secretary of Health and Human Services

(the Secretary), through the establishment of the Smallpox Vaccine Injury Compensation Program (the Program), to provide benefits and/or compensation to certain persons who have sustained injuries as a result of the administration of smallpox covered countermeasures (including the smallpox vaccine) or as a result of vaccinia contracted through accidental vaccinia inoculations. The SEPPA directed the Secretary to establish, by interim final rule, a table identifying adverse effects (including injuries, disabilities, conditions, and deaths) that shall be presumed to result from the administration of or exposure to the smallpox vaccine, and the time interval in which the first symptom or manifestation of each listed injury must manifest in order for such presumption to apply. As mandated by law, the Secretary is establishing such a Smallpox (Vaccinia) Vaccine Injury Table (the Table) through this interim final rule. The Secretary is also establishing a set of Table Definitions and Requirements, which define the terms and conditions included on the Table and are to be read in conjunction with the Table. The Secretary is seeking public comment on the Table established through this interim final rule. At a later date, the Secretary will publish a companion final rule setting forth the administrative implementation of the Program. The public will then be afforded an additional opportunity to comment on the procedures set forth therein.

PMID: 12952013 [PubMed - indexed for MEDLINE]

22: J Clin Microbiol. 2003 Jul;41(7):3154-7.

Improved assay to detect neutralizing antibody following vaccination with diluted or undiluted vaccinia (Dryvax) vaccine.

Newman FK, Frey SE, Blevins TP, Mandava M, Bonifacio A Jr, Yan L, Belshe RB.

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The assessment of immunogenicity of a diluted vaccinia vaccine for possible widespread use of a diluted vaccine in the event of a bioterrorist attack prompted us to focus on the development of a sensitive and specific plaque reduction neutralization (PRN) assay to assess the antibody response of volunteers to a vaccinia (Dryvax) vaccine. Two incubation times, 1 h or overnight (approximately 15 h), were explored for the neutralization step of the assay. In addition, serum samples were evaluated using both sonicated and nonsonicated virus in PRN assays with 1 and 15 h of incubation. The use of the overnight incubation method resulted in the detection of antibody in two vaccinated individuals who exhibited a take, i.e., a major reaction indicative of successive vaccination as defined by the Centers for Disease Control and Prevention, but did not have a fourfold increase in antibody to vaccinia virus by the 1-h-incubation method and increased the sensitivity from 94 to 100%. In addition to the increased sensitivity of the assay, we noted a significant increase (approximately 40-fold) in the PRN titer of serum samples tested with the 15-h-incubation method. The use of sonicated virus increased the reproducibility of the virus titers and PRN titers. Forty-two percent of the samples tested using sonicated virus had a PRN titer that was fourfold higher or greater than that of nonsonicated virus in the assay. A PRN titer that was threefold higher or greater was observed in more than half (58%) of the samples using sonicated virus. Therefore, the more sensitive, specific, and reproducible

plaque neutralization assay for the detection of antibody to vaccinia virus is the method using a 15-h-incubation time and freshly sonicated vaccinia virus.

Publication Types:
Evaluation Studies

PMID: 12843056 [PubMed - indexed for MEDLINE]

23: J Med Biogr. 2003 Aug;11(3):181-2.

Comment on:
J Med Biogr. 2002 Nov;10(4):232-6.

Emmanuel Timonis, Jacobus Pylarinus and inoculation.

Poulakou-Rebelakou E, Lascaratos J.

Publication Types:
Biography
Comment
Historical Article
Letter

Personal Name as Subject:
Timonis ED
Pylarinus J

PMID: 12870046 [PubMed - indexed for MEDLINE]

24: J Postgrad Med. 2003 Apr-Jun;49(2):141-7.

Smallpox: clinical highlights and considerations for vaccination.

Mahoney MC, Symons AB, Kimmel SR.

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Smallpox virus has gained considerable attention as a potential bioterrorism agent. Recommendations for smallpox (vaccinia) vaccination presume a low risk for use of smallpox as a terrorist biological agent and vaccination is currently recommended for selected groups of individuals such as health care workers, public health authorities, and emergency/rescue workers, among others. Information about adverse reactions to the smallpox vaccine is based upon studies completed during the 1950s and 1960s. The prevalence of various diseases has changed over the last four decades and new disease entities have been described during this period. The smallpox vaccination may be contra-indicated in many of these conditions. This has made pre-screening of potential vaccines necessary. It is believed that at present, the risks of vaccine-associated complications far outweigh the potential benefits of vaccination in the general

population.

Publication Types:
Review
Review, Tutorial

PMID: 12867690 [PubMed - indexed for MEDLINE]

25: JAMA. 2003 Sep 17;290(11):1452; author reply 1452.

Comment on:
JAMA. 2003 Jun 25;289(24):3290-4.

Risks of smallpox vaccination.

Fulginiti VA.

Publication Types:
Comment
Letter

PMID: 13129976 [PubMed - indexed for MEDLINE]

26: Lancet. 2003 Aug 23;362(9384):626.

Smallpox: preparation without inoculation.

Nelson K.

Publication Types:
News

PMID: 12947947 [PubMed - indexed for MEDLINE]

27: Minn Med. 2003 Jun;86(6):20-5.

Smallpox vaccination: the Minnesota story.

Golden G.

PMID: 12834209 [PubMed - indexed for MEDLINE]

28: MMWR Morb Mortal Wkly Rep. 2003 Oct 3;52(39):933-6.

Cardiac deaths after a mass smallpox vaccination campaign--New York City, 1947.

Centers for Disease Control and Prevention (CDC).

During the first wave of the 2003 smallpox vaccination campaign, two ischemic cardiac deaths occurred in civilian vaccinees aged 55 and 57 years, and one occurred in a military vaccinee aged 55 years, 4-17 days after vaccination with the New York City Board of Health (NYCBOH) vaccinia strain. Whether these and 13 other recognized military and civilian nonfatal ischemic events among vaccinees were associated with smallpox vaccination is unclear. The same NYCBOH strain was used in 1947 to vaccinate approximately six million New York City (NYC) residents (80% of the population) during a 4-week period (April 4-May 2) after a smallpox outbreak. To determine whether smallpox vaccination increased the risk for cardiac death in 1947, the NYC Department of Health and Mental Hygiene (DOHMH) analyzed data from NYC death certificates during that period. This report summarizes the results of that analysis, which found no increases in cardiac, atherosclerotic, or all-cause deaths. The findings are consistent with a growing body of evidence suggesting that ischemic cardiac deaths observed after the 2003 campaign might have been unrelated to vaccine.

Publication Types:
Historical Article

PMID: 14523370 [PubMed - indexed for MEDLINE]

29: N J Med. 2003 Jul-Aug;100(7-8):47; author reply 47.

Comment on:
N J Med. 2003 Apr;100(4):12-9; quiz 19-22.

State epidemiologist, Eddy Bresnitz, MD, MS, on bioterrorism.

Porwancher R.

Publication Types:
Comment
Letter

PMID: 12955807 [PubMed - indexed for MEDLINE]

30: Occup Health Saf. 2003 Jun;72(6):70-2.

Faster detection & better vaccines.

[No authors listed]

PMID: 12813941 [PubMed - indexed for MEDLINE]

31: Proc Natl Acad Sci U S A. 2003 Aug 5;100(16):9458-63. Epub 2003 Jul 17.

Shared modes of protection against poxvirus infection by attenuated and conventional smallpox vaccine viruses.

Belyakov IM, Earl P, Dzutsev A, Kuznetsov VA, Lemon M, Wyatt LS, Snyder JT, Ahlers JD, Franchini G, Moss B, Berzofsky JA.

Molecular Immunogenetics and Vaccine Research Section, Metabolism Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA. belyakov@mail.nih.gov

The concern about bioterrorism with smallpox has raised the possibility of widespread vaccination, but the greater prevalence of immunocompromised individuals today requires a safer vaccine, and the mechanisms of protection are not well understood. Here we show that, at sufficient doses, the protection provided by both modified vaccinia Ankara and NYVAC replication-deficient vaccinia viruses, safe in immunocompromised animals, was equivalent to that of the licensed Wyeth vaccine strain against a pathogenic vaccinia virus intranasal challenge of mice. A similar variety and pattern of immune responses were involved in protection induced by modified vaccinia Ankara and Wyeth viruses. For both, antibody was essential to protect against disease, whereas neither effector CD4+ nor CD8+ T cells were necessary or sufficient. However, in the absence of antibody, T cells were necessary and sufficient for survival and recovery. Also, T cells played a greater role in control of sublethal infection in unimmunized animals. These properties, shared with the existing smallpox vaccine, provide a basis for further evaluation of these replication-deficient vaccinia viruses as safer vaccines against smallpox or against complications from vaccinia virus.

PMID: 12869693 [PubMed - indexed for MEDLINE]

32: RN. 2003 Jul;66(7):52-8; quiz 60.

Smallpox vaccine: the reality, the risk.

Taccetta-Chapnick M.

Victory Memorial Hospital in Brooklyn, N.Y., USA.

Publication Types:
Review
Review, Tutorial

PMID: 12900999 [PubMed - indexed for MEDLINE]

33: Tenn Med. 2003 Aug;96(8):377-9.

Tennessee prepares for the threat of smallpox.

McIntyre PS.
Tennessee Department of Health, Nashville, USA.

PMID: 12971074 [PubMed - indexed for MEDLINE]